

August 14, 1959

Dr. Emil L. Smith  
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Dear Emil:

What would you say to the guess that the specific carbohydrate you are finding in globulin is the specific receptor for complement? Complement fixation has always puzzled me since it did not easily make sense that it should depend on the interaction between antibody and antigen but the nature of the antigen was immaterial. But suppose it is some common element in all antibody which recognizes complement but the binding energy of a single antibody molecule with complement is insufficient to make a stable complex. However, complexes consisting of at least 2 antibody molecules stabilized by their reaction with a common antigen, might then have the further capacity to bind complement between them. If there is such a common element among all antibodies, it seemed to me that your carbohydrate might be a plausible candidate. Complement then becomes a sort of antibody to the globulin-carbohydrate; perhaps further, the same carbohydrate or a related one is the cell-wall-element which is the substrate for the enzymatic action of complement. Anyhow, if you haven't already done this, the hunch does suggest one of a great many tests to make on the carbohydrate fraction. Another point that might be pertinent I am not clear on: the extent of fixation of complement by soluble antigen-antibody complexes where the postulated condition of two adjacent antibody molecules would not be met.

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Yours sincerely,

Joshua Lederberg

Encl.